

REMARKS

Reconsideration is respectfully requested. Claims 19-23, 26-36 are pending. Claims 24 and 25 are canceled. Claims 19 and 20 are amended. No new matter has been added due to the amendments. Amendment to and cancellation of the claims does not affect inventorship.

Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Rejection Under 35 USC § 112, First Paragraph

The Office Action has rejected Claims 19 and 21 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. In view of the remarks made herein, the Applicants respectfully request that this rejection be withdrawn.

The Applicants assert that the specification provides adequate written description support for the claimed subject matter of Claims 19 and 21. In particular, the Applicants respectfully submit that the specification provides abundant written description support for practicing the claimed invention. In particular, the Applicants note that the specification provides support for the amino acid moieties and exemplary methods of testing the compounds at, for example, page 23 line 20 through page 24, line 40, and resulting exemplary species of the claimed genus at, for example, table 1 page 68.

Furthermore, the specification provides working examples demonstrating exemplary synthesis protocols for generating the compounds, at pages 57, 58, 59, as noted in the Office Action, and examples of generated compounds at table 1 page 68.

In view of the above it is submitted that the claims do comply with the written description requirement. The specification provides multiple representative examples, including working

examples of representative MRI compounds, such that one of skill in the art would have no doubt that the Applicants were in possession of the invention as claimed at the time the application was filed. Therefore, this rejection may be withdrawn.

Rejection Under 35 USC § 112, Second Paragraph

The Office Action has rejected Claims 19 and 21 under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps. Claim 19 has been amended to include “producing a magnetic resonance image of a cell, tissue, or patient”. Therefore, this rejection may be withdrawn.

The Office Action has rejected Claims 20, 22, 25 and 29 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Office Action asserts that description of “linker” for X₂ is confusing since it occupies a terminal position. Claim 20 has been amended to remove the objectionable language. Therefore, this rejection may be withdrawn.

Rejection Under 35 USC § 102

Claims 20, 22, 25 and 29 are rejected under 35 U.S.C. § 102(e) for allegedly being anticipated by U.S. Patent No. 6,709,646 (Lauffer *et al.*). In view of the amendments to the claims and the remarks made herein, the Applicants respectfully request that this rejection be withdrawn.

The present claims are directed to a method of administering an activatable MRI agent comprising a chelator and a paramagnetic metal ion that is coordinatively saturated by the chelator and a covalently attached MMP active peptide. Upon cleavage of the MMP active peptide the T₁ of the claimed MRI agent is decreased thereby providing a magnetic resonance image.

The Office Action asserts that Lauffer teaches a “preferred method of bioactivating the contrast agents includes the enzymatic cleavage of the prodrug at the MS (column 5, lines 49-50)” (Office Action, page 5)”. However, the Applicants note that reference to “bioactivation” in Lauffer is with respect to increasing the binding affinity of the protein binding moiety of the compound to the target or substrate (see column 5, line 53-57).

As such, the Applicants respectfully disagree that Lauffer teaches cleavage of the MS (modification site) and any subsequent decrease of the T₁ of the MRI agent following a cleavage event as presently claimed. There is no indication in Lauffer that cleavage of the MS would result in a decrease in the T₁ of the IEM (image enhancing moiety). There is no further disclosure in Lauffer with respect to cleavage of the MS and the remaining composition following administration of the compound and any subsequent change in T₁ of the chelator.

Even if, *in arguendo*, the MS compound is cleaved and released from the composition described in Lauffer, there is no teaching that the T₁ of the chelator would change. In fact, if the MS is cleaved from the Lauffer compound, the PMB would remain linked to the chelator (see column 4, lines 59-61). Therefore, there is no expectation that the T₁ of the Lauffer compound would behave in a similar manner as the compound of the present claims.

The Applicants respectfully submit that the components of the claimed invention possess a unique functional characteristic that is not present in the prior art, i.e., a change in T₁ of the MRI agent following cleavage of the MMP active peptide.

In *In Re Swinehart*, the court held that a composition of matter claim with a functional limitation was proper where it constituted the point of novelty between the applicants’ claim and the prior art. The claim at issue in *Swinehart* read “[a] new composition of matter, transparent to infra-red rays and resistant to thermal shock, the same being a solidified melt of two components ...” *Id.* at 227. In particular, the novel limitation, “transparent to infra-red rays,” was rejected by the Examiner and the Board as improper functional language. *Id.* at 227-28. The C.C.P.A. disagreed, explaining that:

Our study of these cases ... satisfies us that any concern over the use of functional language at the so-called ‘point of novelty’ stems largely from the fear that an applicant will attempt to distinguish over a reference disclosure by emphasizing a property or function which may not be mentioned by the reference and thereby assert that this

claimed subject matter is novel. Such a concern is not only irrelevant, it is misplaced ... [W]here the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on. *Id.* at 228-29.

In the instant case, the Applicants have claimed a method of using a composition of matter using the functional limitation when the “MMP active peptide is cleaved...the T₁ of said MRI agent is decreased” as a point of novelty distinguishing the claims from the prior art. There is no indication that Lauffer possesses this characteristic. In contrast, the novelty of the instant invention stems from the fact that cleavage of the cleavage site is required to cause the T₁ of the MRI agent to change.

Since Lauffer fails to teach cleavage of the MMP active peptide from the composition and subsequent change in T₁ in order to turn “on” the chelator, it fails to teach each and every element of the claims. Therefore, the cited reference cannot anticipate the present invention. In addition, the functional point of novelty is not inherent in Lauffer. Consequently, under *Swinehart* the Applicants’ use of functional language properly distinguishes the claims from the prior art. *See Swinehart* at 228-29. The Applicants therefore respectfully request that the rejection be withdrawn on these grounds.

Rejection Under 35 USC § 103

Claims 19-22, 25 and 29 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,709,646 (Lauffer *et al.*) in view of Netzel-Arnett *et al.* (*Biochem.*, 1993, 32, p. 6427-6432). In view of the amendments to the claims and the remarks made herein, the Applicants respectfully request that this rejection be withdrawn.

When rejecting claims under 35 U.S.C. § 103(a), the Patent Office bears the burden of establishing a *prima facie* conclusion of obviousness. In order to do so, the Patent Office must demonstrate three elements: (1) that the prior art provides a suggestion or motivation to modify or combine the teachings of the references relied upon by the Office to reject the claims; (2) that the prior art provides one of skill in the art with a reasonable expectation that the suggested

combination or modification would be successful; and (3) that the prior art, either alone or in combination, teaches each and every limitation of the rejected claims. The teaching or suggestion to make the claimed invention and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). These three elements are distinct. If any one elements is not established, *prima facie* obviousness is not established.

As noted above Lauffer fails to teach cleavage of the MMP active peptide from the composition and subsequent change in T_1 in order to turn "on" the chelator. Netzel-Arnett has been cited for teaching specific MMP peptides. However, it fails to make up the deficiency of Lauffer because it also fails to teach activatable chelator that exhibits a change in T_1 in order to turn "on" the chelator.

Therefore, in combining the cited references, there is no teaching of an activatable MRI agent comprising a chelator and a paramagnetic metal ion that is coordinatively saturated by the chelator and a covalently attached MMP active peptide, where upon cleavage of the MMP active peptide the T_1 of the claimed MRI agent is decreased thereby providing a magnetic resonance image. Since the combination of cited references fails to teach each and every limitation found in the claims, the cited references cannot render the present claims obvious. As such, the Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-442-1000.

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